## REMARKS

By the present communication, Claims 1-9, 18 and 38-42 are pending. Claims 10-17 and 19-37 have been canceled. Applicants expressly reserve the right to pursue the subject matter of these claims in a timely filed continuation application. Claims 1-9 and 18 have been amended and Claims 38-42 have been added to define Applicants' invention with greater particularity. No new matter is introduced as the amended and new claim language is fully supported by the specification and claims as originally filed. In view of the amendments and the following remarks, Applicants respectfully request reconsideration of the claims and submit that the present application is now in condition for allowance.

### I. Rejections Under 35 U.S.C. § 112, 2nd Paragraph

Applicants respectfully traverse the rejection of Claims 1-37 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically it was asserted in the Office Action that in Claim 1, the terms "C-amido" and "sulfonyl" as used in $R^1$ and the terms "sulfinyl," "sulfonyl," and "sulfonamido" as used in $R^3$, $R^4$, $R^5$ and $R^6$ are allegedly ambiguous. Applicants disagree.

Applicants note first that cancellation of Claims 10-17 and 19-37 has rendered the rejection moot with respect to these claims. Applicants also note that minor typographical errors have been corrected in the definition of $R^8$ in Claim 1.

Applicants respectfully submit that the term "C-amido" is clear as written. Indeed, Applicants clearly define this term on page 23 of the application. Accordingly, those of skill in the art will readily appreciate that, as used in the present claims, the term "C-amido" refers to a $-C(=O)NR^{10}R^{11}$ group where $R^{10}$ and $R^{11}$ are defined in the claims themselves. Moreover, the Examiner's concern regarding the attachment point of the C-amido group is misplaced. The definition of "C-amido" provided by Applicants in the specification clearly shows the carbon of the C-amido group to which the core structure of Formula I is attached. To the skilled artisan, it

does not matter whether the C-amido group is attached to a carbon or nitrogen of the core structure, or whether the name of the combined moiety might be other than an amide, so long as the identity of the complete structure is clear. Applicants therefore submit that based on the definition provided, the skilled artisan will readily appreciate the identity of a compound of Formula I bearing a C-amido group at any particular variable such as $R^1$.

Applicants likewise submit that the term "sulfonyl" in the definition of $R^1$ in Claim 1 and the terms "sulfinyl," "sulfonyl" and "sulfonamido" in the definition of $R^3$, $R^4$, $R^5$, and $R^6$ in Claim 1 are clear as written. The terms "sulfonyl" and "sulfonamido" are defined on page 23 and the term, "sulfinyl" is defined on page 22 of the application. Applicants respectfully submit that the attachment point and substituents on these functional groups will be readily appreciated by those of skill in the art for the same reasons that the C-amido group will be understood by those of skill in the art.

Accordingly, Applicants, respectfully request the withdrawal of the rejection of claims 1-37 under 35 U.S.C. § 112, paragraph 2 based upon the terms "C-amido," "sulfinyl," "sulfonyl," and "sulfonamido".

Applicants respectfully traverse the rejection of Claims 1, 10, 18 and the claims which depend therefrom as allegedly indefinite for containing the term "prodrug." Although Applicants respectfully disagree with this assertion, the term "prodrug" has been removed from each claim in which it appeared. This amendment has been made solely to advance prosecution in a timely manner and Applicants expressly reserve the right to pursue this subject matter in a timely filed continuation application. Applicants, therefore, respectfully request that the rejection under 35 U.S.C. § 112, paragraph 2 based upon the recitation of "prodrug" in the claims be withdrawn.

Claim 9 has been amended to add the word "and" at the proper position of each Markush group from which it was missing. Accordingly, Applicants respectfully request the withdrawal of rejection of Claim 9 under 35 U.S.C. § 112, paragraph 2 for lacking the word "and."

The rejection of Claims 11, 12, 14, 16, 20, 21, 23, 25, 28, 30, 31, 32, 34, and 35 as allegedly indefinite for reciting the word "comprises" is rendered moot by the cancellation of these claims. It is respectfully requested that this rejection be withdrawn.

## II. Rejections Under 35 U.S.C. § 112, 1st Paragraph

Applicants respectfully traverse the rejection of Claims 1-37 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Claims 10-17 and 19-37 have been canceled, thus rendering the rejection moot for these claims. Of the remaining claims, 1-9 and 18 stand rejected as allegedly not enabled for making prodrugs of the claimed compounds. Although Applicants respectfully disagree with this assertion, Claims 1-9 and 18 have been amended to delete the term "prodrug" solely to advance prosecution in a timely fashion. Applicants expressly reserve the right to pursue this subject matter in a timely filed continuation application. It is respectfully requested that the rejection of Claims 1-9 and 18 under 35 U.S.C. § 112, first paragraph be withdrawn.

Claims 10-17 stand rejected as allegedly lacking enablement for the "modulation of any or all receptor or non-receptor protein kinases generically embraced in claim language and protein kinase modulation by prodrugs of the claimed compounds." (Office Action, page 7.) Claims 10-17 have been canceled, rendering the present rejection moot. New Claim 38 is directed to the modulation of the catalytic activity of a protein kinase wherein the protein kinase is selected from EGF, HER2, IGF-1R, PDGFRα, PDGFRβ, Flk-1R, Met, Src, Lck, CDK2 and Raf. The recited kinases are those which the Examiner has specifically identified as enabled on pages 101-160 of the specification. Accordingly, Applicants respectfully submit that Claim 38 is fully enabled and, therefore, patentable.

Claims 19-37 stand rejected as allegedly lacking enablement for "treating or preventing any or all disorders/disease related to protein kinase generally embraced in claim language." (Office Action, page 10.) Claims 19-37 have been canceled, rendering the rejection moot with respect to these claims. Applicants expressly reserve the right to pursue the canceled subject

matter in a timely filed continuation application. New Claims 39-42 are directed to methods for treating a protein kinase related disorder that is an angiogenesis related disorder. Claim 40 specifies that the angiogenesis related disorder is breast cancer. The recited disorders are those which the Examiner specifically indicated were enabled by the present application. Accordingly, Applicants respectfully submit that Claims 39-42 are fully enabled and, therefore, patentable.

## III. Rejections Under Obviousness-type Double Patenting

The Office Action rejects Claims 1-37 under the judicially created doctrine of obviousness – type double patenting alleging that these claims are unpatentably obvious over the following patent claims:

| Patent No. | Claims in Cited Art | Rejected Claims |
|---|---|---|
| 6,677,368 ('368) | 1-19 | 1-3, 6-8, 10-37 |
| 6,642,232 ('232) | 1-25 | 1-3, 6-8, 10-37 |
| 6,635,640 ('640) | 1-13 | 1-4, 6-9, 18 |
| 6,486,185 ('185) | 1-40 | 1-37 |
| 6,395,734 ('734) | 1-23 | 1-3, 6-8, 10-37 |
| 6,316,635 ('635) | 1-29 | 1-37 |
| 6,313,158 ('158) | 1-21 | 1-37 |

As acknowledged in the Office Action, a terminal disclaimer may be used to overcome an actual or provisional rejection based on non-statutory double patenting. Applicants note that because Claims 10-17 and 19-37 have been canceled, the rejections of those claims are rendered moot. With respect to remaining Claims 1-9 and 18, Applicants respectfully submit that the present obviousness type double patenting rejections are improper.

The Office Action simply fails to set forth a sufficient basis for these rejections. As required by the Federal Circuit (*In re* Longi, 225 USPQ 645, 651 (Fed. Cir. 1985)) and stated in the MPEP, the analysis in an obviousness-type double patenting determination parallels the guidelines for a 35 U.S.C. 103(a) rejection. § 804 II. B. 1. Moreover:

> Any obviousness-type double patenting rejection should make clear:
>
> (A) The differences between the inventions defined by the conflicting claims –a claim in the patent compared to a claim in the application; and
>
> (B) The reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim in issue is an obvious variation of the invention defined in a claim in the patent.
>
> *Id.*

Applicants respectfully submit that the analysis set forth in the Office Action does not follow that required for an obviousness rejection and does not meet the requirements laid down by the Patent Office in § 804 II. B. 1. quoted above. Thus, the Office Action fails to identify for any cited claim, the motivation for one of ordinary skill in the art to select the chemical genus or subgenuses of the present invention. Instead, the Examiner picks and chooses among the variables in the chemical genuses of the cited patents to construct subgenuses allegedly embraced by the present claims. Even where accurate—and there are a number of instances where it is not—such picking and choosing of variables reveals nothing about the obviousness of the invention as a whole.

For example, the '635 patent claims do not define and cannot fairly suggest the chemical genus/subgenuses of the present claims. The claims of the '635 patent are directed to various imidazolyl-methylidenyl-indolinones. Contrary to the assertion on page 17 of the Office Action, such compounds lie outside the scope of at least present Claims 2-8, none of which include imidazolyl-methylidenyl-indolinones. Moreover, Claims 1 and 9 define numerous compounds that lie outside the scope of the claims of the '635 patent, including but not limited to those where $R^1$ is not H; or where M and L are independently C, O or S; or where J is O or S; or where K is N, O, or S; or where $R^7$ is C-amido, guanyl, or sulfonyl; or where $R^8$ is a five member cycloalkyl, aryl, heteroaryl or heteroalicyclic ring fused to two adjacent atoms of the Q ring. Conversely, the '635 patent defines numerous compounds that lie outside the present claims

including, but not limited to, those where $R_6$ and $R_7$ or $R_7$ and $R_8$ or $R_8$ and $R_9$, combined, may form a five member aromatic or heteroaromatic ring group or a five or six member alicyclic or heteroalicyclic ring group. Accordingly, one of ordinary skill will understand that the very different focus of the claims of the '635 patent from the present claims cannot render the latter obvious.

Likewise, the pyrrolyl and imidazolyl indolinones of the '368, '232, '640, and '734 patents fail to teach or suggest the full scope of the present claims for the same reasons. For example, claims 1-19 of the '368 patent define various 4-aryl substituted indolinones. Contrary to the assertion on page 15 of the Office Action, such compounds lie outside the scope of at least present Claim 7, which does not include 4-aryl-indolinones. Furthermore, Claims 1-3, 6 and 8 define numerous compounds that lie outside the scope of the claims of the '368 patent, including, but not limited to, those where $R^1$ is alkyl, cycloalkyl, aryl, hydroxy, alkoxy, carboxyl, C-amido or sulfonyl; or where $R^3$ is hydrogen, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, thiohydroxy, thioalkoxy, thioaryloxy, sulfinyl, sulfonyl, sulfonamido, carbonyl, carboxyl, cyano, nitro, halo, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, C-amido, N-amido, amino or $-NR^{10}R^{11}$; or where $R^4$, $R^5$, and $R^6$ are independently alkenyl, alkynyl, heteroaryl, heteroalicyclic, carbonyl, carboxyl, cyano, nitro, O-carbamyl, N-carbamyl, O-thiocarbamyl, or N-thiocarbamyl; or where $R^3$ and $R^4$, $R^4$ and $R^5$, or $R^4$ and $R^5$ may combine to form a six-member aryl or heteroaryl ring; or where J is O or S; or where M, L, and K are independently N, O, or S. Plainly, the extent of these differences render the present claims nonobvious over the '368, '232, '640, and '734 patents.

Similarly, nonobvious differences exist between the compounds defined by the present claims and those defined in the '158 and '185 patents. Contrary to the assertion on page 17 of the Office Action, at least the imidazolyl-substituted indolinones of Claim 9 lie beyond the scope of the compounds defined in the '158 patent. Other claims of the present invention define numerous compounds that lie outside the scope of the claims of the '158 patent, including, but not limited to, those where $R^2$ is heteroaryl or heteroalicyclic; or where at least one of M, L, and

K are N, O, or S; or where $R^8$ is O-carbamyl or N-carbamyl. Conversely, the '158 patent defines numerous compounds not defined by the present claims including, but not limited to, those where Z is S or $NR^{11}$; those where $R^{11}$ is alkyl, cycloalkyl, aryl, hydroxy, alkoxy, aryloxy, R"C(O)-, -C(O)OR", R"C(O)O-, C-amido, guanyl, fulfonyl, or trihalomethanesulfonyl; or where $R^1$ is alkenyl, alkynyl, trihalomethane, R"C(O)-, or trihalomethanesulfonyl; or where $R^2$ is halogen. Likewise, the present claims define but a small fraction of the compounds embraced by the '185 patent. The present Office Action fails to address the inventions defined by the cited patent on a claim by claim basis as required, and fails to point to any motivation to modify the cited claims to yield the invention defined by the present claims.

For all the reasons given above, it is requested that the obviousness-type double patenting rejections of Claims 1-9 and 18 be withdrawn. Because the new claims 38-42 depend directly or indirectly on Claim 1, it is respectfully submitted that they are free of the double patenting rejection as well.

## CONCLUSION

In view of the above amendment and remarks, reconsideration and favorable action on all claims are respectfully requested. If any issues remain to be resolved in view of this response, the Examiner is invited to contact the undersigned at the telephone number set forth below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

Date December 10, 2004

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